

# 2012 American Society of Health-System Pharmacists Midyear Clinical Meeting & Exhibition

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The 47th American Society of Health-System Pharmacists Midyear Clinical Meeting & Exhibition in early December took place in Las Vegas, Nevada, with a record-breaking attendance of more than 20,000 registrants. Some themes of the program addressed enhancing medication safety through different uses of technology and knowledge, fine-tuning clinical skills, dealing with drug shortages, pharmacy practice model initiatives, Section 340B drug program policies, and the use of biologics in health care. This article reviews two sessions, one on preparing for generic biologics (e.g., biosimilars) and one on medication safety related to the Joint Commission's hospital accreditation standards.



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## Preparing for Biosimilars: Scientific, Regulatory, and Practice Management Issues for Pharmacists

- Edward Li, PharmD, BCOP, Associate Professor, Department of Pharmacy Practice, University of New England College of Pharmacy, Portland, Maine
- James G. Stevenson, PharmD, Chief Pharmacy Officer, University of Michigan Health System; and Professor and Associate Dean for Clinical Sciences, University of Michigan College of Pharmacy, Ann Arbor, Michigan
- James M. Hoffman, PharmD, MS, BCPS, Program Chair, Medication Outcomes and Safety Officer, St. Jude Children's Research Hospital; and Associate Professor of Clinical Pharmacy, College of Pharmacy, University of Tennessee Health Science Center, Memphis, Tennessee

Biologic agents are integral in the care of patients worldwide, and many of these agents have been included in the top 15 drug expenditures in clinics in the U.S. over the past few years. The future availability of generic biologics is not yet clearly defined because of their complex molecular structure, their complicated manufacturing processes, and their high cost. However, the potential of biosimilars to provide cost competition and a lower price was the impetus behind the Biologics Price Competition and Innovation Act of 2009 (BPCI), a part of the 2010 Affordable Care Act (ACA). The structure of an abbreviated approval pathway was included in the BPCI. In

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addition, because biologics and biosimilars are essential to cancer care, the National Comprehensive Cancer Network (NCCN) has been very active and developed a white paper on how to incorporate biosimilars into clinical practice. Much of the information presented at the ASHP symposium was derived from the NCCN experience.

New definitions have been developed and are essential to understanding biosimilars; however, the definitions have varied. The FDA has published a number of definitions in a draft guidance for industry (see Suggested Readings). Following are some examples of terminology:

- A *biosimilar* is a biologic that has been deemed to be "highly similar" to a reference biologic; there are no clinically meaningful differences.
- A *reference product* is the product to which the biosimilar is being compared (such as a current brand-name biologic agent).
- *Biosimilarity* means that there is no "clinically meaningful" difference between the biosimilar and the reference product. The two molecules are different but have *highly similar* effects on safety and efficacy.
- *Bioequivalence* is the absence of a significant difference in the rate and extent to which active ingredients are available at the action site when administered at the same molar dose under similar circumstances in an appropriately designed study.
- Biosimilarity and bioequivalence are not the same thing, and the terms cannot be interchanged.

No *clinically meaningful* differences are wanted between the biosimilar and the reference product; this is because these molecules are complex with high molecular weights, undergo different manufacturing and production processes, and have a higher potential for immunogenicity. In many instances, the manufacturing steps are proprietary; therefore, the manufacturing process for biosimilars must be validated. Even a small alteration could result in a different end-product. Therefore, assessing biosimilarity is a complicated process.

Without reproducing randomized clinical trials and using smaller-scale direct comparisons and extrapolations instead, the sponsor of the biosimilar product must provide evidence that the candidate drug does not differ significantly from the reference product. All available evidence, including laboratory data, comparative animal toxicology data, and *in vitro* or *in vivo* studies of pharmacological activity, must be evaluated before a regulatory decision can be made. Human pharmacokinetic and pharmacodynamic data are essential to prove biosimilarity. To compare clinical immunogenicity, the FDA usually recommends a comparative parallel study.

Ultimately, only postmarketing pharmacovigilance and clinical studies can provide evidence of comparability related to

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safety and efficacy. The FDA may issue general or specific guidelines, including postmarketing surveillance. After approval of the biosimilar product, tracking and surveillance, efficacy and safety, P&T committee decisions, and financial costs must still be considered. Despite the complexities of biosimilar development, the pathway to approval should become more transparent.

### Top 10 Medication Safety Issues Related to the Joint Commission Hospital Accreditation Standards

• Darryl S. Rich, PharmD, MBA, Medication Safety Specialist, Institute for Safe Medication Practices, Horsham, Pennsylvania

In his talk from the perspective of a safety expert and a former surveyor at the Joint Commission in Oakbrook Terrace, Illinois, Dr. Rich discussed key safety issues that correspond directly to Joint Commission medication standards. Including examples and strategies for improving effectiveness for Joint Commission reviews, he noted that hospitals have been consistently noncompliant in several elements of performance:

- failing to remove expired drugs
- not implementing procedures for high-alert and hazardous medications
- failure of pharmacists to review all medication orders before dispensing
- compounding or mixing sterile preparations in non-urgent situations by pharmacy personnel only (exceptions to non-pharmacy preparation should be rare)
- not having emergency medications readily available in patient-care areas
- not taking appropriate action to avoid errors with the interchange of look-alike–sound-alike (LASA) drugs
- failing to reconcile medications before patient admission with those drugs ordered upon patient admission
- failing to label medication doses when a drug is prepared but not administered immediately

Some of the reasons stated for continued Joint Commission noncompliance included:

- difficulty implementing or sustaining changes in procedures
- citing problems that are considered beyond the pharmacy department's control
- pharmacies that are overwhelmed, thereby lacking the ability to prioritize and to make timely efforts to improve performance
- making quick fixes that do not resolve problems in the long run but rather make the problems even worse

Dr. Rich noted that a high-alert medication list should incorporate more than just the institution's LASA drugs. Some drugs (e.g., concentrated electrolytes, neuromuscular blockers, opioids, anticoagulants, insulin, and cancer chemotherapeutic agents) should always be included. To develop a list, the current

medical or pharmaceutical literature should be reviewed to identify agents that need to be included. Each institution then needs to evaluate its internal medication error-reporting data by determining which drugs are involved in the most errors. These identified medications should then be added to the high-alert list if they are not already there. The list also needs to be flexible so that changes can be made as needed. Appropriate actions for high-alert medications need to be implemented.

Dr. Rich also suggested implementing the following safety principles:

- limiting medication access by restricting access to specific practitioners
- differentiating products (e.g., with Tall-Man lettering and color coding)
- segregating similar products during storage (e.g., separating LASA drugs with similar dosages)
- storing only certain dosage strengths or concentrations (e.g., opioids)
- independent double-checking by nurses and pharmacists
- using standardized order forms, protocols, and guidelines
- not allowing verbal orders

These steps should help institutions improve their medication-management systems to help meet Joint Commission standards.

### Suggested Readings

FDA. *Guidance for Industry: Biosimilars Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009*. February 2012. Available at: [www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidance/UCM273001.pdf](http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidance/UCM273001.pdf). Accessed December 21, 2012.

Rich DS. At the time of this writing, a free copy of Dr. Rich's talk was available at the ASHP Web site, <https://quickstart.quickmobile.com/cms/resources/render/787/1/633>. Accessed January 2, 2013.

Zelenetz AD, Ahmed I, Braud EL, et al. NCCN Biosimilars White Paper: Regulatory, Scientific, and Patient Safety Perspectives. *J Natl Compr Canc Netw* 2011;9:S-1–S-22. Available at: [www.nccn.org/JNCCN/supplements/PDF/2011\\_Vol9\\_Suppl\\_4\\_Biosimilars.pdf](http://www.nccn.org/JNCCN/supplements/PDF/2011_Vol9_Suppl_4_Biosimilars.pdf). Accessed January 2, 2013.

The work group identified challenges surrounding biosimilars, including health care provider knowledge, substitution practices, pharmacovigilance, naming and product tracking, coverage and reimbursement, use in off-label settings, and data requirements for approval. ■